

Remarks/Arguments:

Claims 1-12 were pending in the application at the time of the Office Action. Claim 1 is amended to clarify that the process is a preparative separation process that is capable of providing at least 0.1 gram of the separated (-)- Δ^9 -trans-tetrahydrocannabinol in less than a day, as supported on page 2 of the application at lines 27-30. New claim 13 is added, as supported at the same passage.

The specification is amended to correct an obvious error in the characterization of U.S. Pat. No. 6,403,126 to Webster et al. Explanation of the need for correction is provided further below, and no new matter has been added.

35 USC § 101

Claims 1-7 and 12 are rejected under 35 USC § 101 as inoperative and therefore lacking utility. The Examiner asserts that the rejected claims require recitation of a further chromatographic step, citing Comparative Example 1 as proof. Applicants respectfully disagree, and note that the Examiner's argument is based on an incorrect premise that this example uses carbon dioxide as the mobile phase. It does not use carbon dioxide; rather, it uses hexane/ethanol, and it is this eluent that fails to separate (-)- Δ^9 -trans-THC from the DPA-Iso impurity. This comparative example contrasts with the Examples according to the invention, all of which use carbon dioxide. Applicants can find no teaching in the specification indicating that a further chromatographic step using an achiral stationary phase is necessary, and respectfully request that the rejection be withdrawn.

35 USC § 103(a)

Claims 1-12 are rejected under 35 USC § 103(a) as unpatentable over any of Cole, Backstrom, and Later, each in view of Levin.

The Examiner argues, in essence, that it would have been obvious at the time of invention to purify (-)- Δ^9 -trans-THC using a derivatised polysaccharide stationary phase as taught by Levin in combination with use of CO₂ as an eluent, as taught by any of Cole, Backstrom, or Later.

Applicants traverse the rejection for the following reasons. The technical problem solved by the present invention is the provision of sufficient quantities of enantiomerically pure (-)- Δ^9 -THC for incorporation into pharmaceutical products (page 1 of the PCT specification, lines 30 - 32). This technical problem is solved by the process specified in amended claim 1, which now recites

a preparative separation process that is capable of producing at least 0.1g of separated (-)- Δ^9 -THC in less than a day. In contrast, Cole relates to the analysis of cannabis by supercritical fluid chromatography, using ultraviolet detection (see title). The mobile phase is disclosed as being CO₂ and methanol, and the stationary phase is a cyanopropyl silica column (see "Materials", page 146, points 7 and 8).

Amended claim 1 differs from Cole in at least two respects. Firstly, the stationary phase does not comprise a derivatised polysaccharide (as noted by the Examiner) and, secondly, the chromatographic method is not a preparative one. The latter point is established by the fact that the authenticated cannabinoid standards are prepared at a concentration of 1mg/mL in ethanol (see "Materials", page 146, point 1) and the analysed cannabis products are prepared at a concentration of 10mg/mL ("Method", page 146, point 2). These concentrations are very much smaller than would be needed to produce the quantities of product capable of being obtained in according to the invention, and thus, there is no indication that the method of Cole can be used as a preparative process capable of producing at least 0.1g of product in less than a day as presently claimed.

Levin relates to the analytical separation of six pairs of chiral cannabinoids using a dimethylphenylcarbamate derivative of amylose, immobilised on silica gel (ChiralPak AD), using 2-propanol and ethanol as the modifiers of *n*-hexane in the mobile phase (see abstract). Like Cole, Levin teaches only an analytical separation (see page 56, 1st column, final paragraph, where 0.1mg of analyte is dissolved in 1mL of the appropriate solvent). Thus, Levin et al. does not remedy Cole's deficiency of not providing at least 0.1 gram of product in less than a day.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Further, as noted in MPEP 2143.03, "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970).

Since at least the claim element reciting a process capable of producing at least 0.1g of product in less than a day is not taught or suggested by the combined references, *prima facie* obviousness has not been established and the rejection should be withdrawn.

Backstrom et al. relates to the analysis of cannabis by supercritical fluid chromatography with atmospheric pressure chemical ionisation mass spectroscopic detection (see title). The chromatographic column utilized in this method is a cyanopropyl silica packed column (page 93,

column 1, second paragraph). Like the other cited references, Backstrom et al. relates to an analytical chromatographic technique, not a preparative one, as evidenced by the fact that the cannabinoid standards and the herbal drug material studied are prepared at a concentration of 10mg/mL in ethanol (page 92, 2nd column, "Materials").

Claims 1-12 are not obvious over Backstrom et al. in combination with Levin et al. for the same reasons as discussed above, i.e., a preparative separation process is neither taught nor suggested. Moreover, applying the methods of Backstrom et al. in attempting to obtain at least 0.1g of product in less than a day would fail, because the product would in fact be destroyed during Backstrom's chemical ionisation mass spectroscopic detection step.

Later et al. relates to the analysis (not preparative separation) of various classes of drugs by capillary supercritical fluid chromatography (see title). The stationary phase utilized is a methylpolysiloxane column in conjunction with a flame ionisation detector (abstract).

Later et al. teaches nothing further than what is already known with regard to Backstrom et al, namely, an analytical chromatographic method using a detection step which destroys the sample, thereby making it incapable of producing at least 0.1g of product in less than a day as claimed. Accordingly, the pending claims are not obvious over Later et al. in combination with Levin et al. for the reasons discussed above in relation to Backstrom et al. and Levin et al.

Claims 1-12 are rejected under 35 USC § 103(a) as unpatentable over US Pat. No. 6,403,126 ("Webster") in view of Levin. The Examiner asserts that Webster discloses the combination of carbon dioxide extraction and column chromatography in the purification of Δ^9 -tetrahydrocannabinol. Applicants note that Webster relates to a method of extracting cannabinoids, cannflavins, and/or essential oils from hemp, as well as producing a whole hemp product lacking Δ^9 -THC (abstract). The document describes how the cannabis chaff is extracted with either a solvent (column 4, lines 26-48) or a supercritical fluid optionally containing an organic modifier such as methanol (column 4, line 49 – column 5, line 2). The resulting extract is then passed through a chromatographic column (column 5, lines 3-4). As is known in the art, supercritical fluid extraction does not involve passing the material to be separated through a stationary phase, and such a method is therefore distinct from supercritical fluid chromatography, which does employ a stationary phase. Webster teaches the use of supercritical carbon dioxide for extraction, but not for chromatography. Rather, in situations where Δ^9 -THC is to be separated from related compounds such as cannabinoids and cannflavins,

Webster directs the skilled person to use HPLC with a reversed phase C₁₈ column and a mobile phase of, for example, acetonitrile and water or methanol and water (Example II).

Thus, despite having mentioned carbon dioxide as one of many suitable solvents for use as an extractant for isolating a mixture of cannabinoids from chaff, Webster does not teach or suggest that it may be used as an eluent for a chromatographic method that allows separating components of that mixture from each other as presently claimed. Levin does not remedy Webster's deficiency in this respect, and thus, not all of the claim elements are taught. Accordingly, the claims are not *prima facie* obvious over Webster in view of Levin, and the rejection should be withdrawn.

Applicants further submit that the Examiner's obviousness rejections are based on the use of impermissible hindsight. As the person skilled in the art would be aware, the development of a chromatographic method for the separation of one compound from a mixture of other compounds is highly dependent on both the stationary and mobile phases. An eluent that is appropriate for separating any given compound from others using a particular stationary phase is often unsuitable for use on a different stationary phase. Because of this, the skilled person understands that the stationary phase of one method cannot be taken out of context with its reported mobile phase. Likewise, a reported mobile phase cannot be considered in isolation from the accompanying teachings relating to the choice of appropriate stationary phase. Accordingly, Applicants submit that it is improper for the Examiner to pick and choose various features from the prior art documents without taking the entire teaching into context. "A prior patent must be considered in its entirety, i.e., as a whole, including portions that would lead away from the invention in suit." *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1575 (Fed.Cir.1987). In the present situation, given the complex and unpredictable interactions between an eluent and a stationary phase, between the stationary phase and each of the compound to be separated, and between each of those compounds and the eluent, there would have been no reasonable expectation of success in trying to separate Δ^9 -THC using carbon dioxide as taught by Cole, Backstrom, and Later on the completely different stationary phase taught by Levin.

References

The Examiner has requested clearer copies of Cole, Backstrom et al, Later et al. and Levin et al. Enclosed are copies that have been scanned at high resolution and that are the clearest copies available to Applicants.

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Conclusion

Applicants submit that the rejections have all been overcome, and respectfully request reconsideration and allowance of the pending claims. Applicants invite the Examiner to contact their undersigned representative, Frank Tise, if it appears that this may facilitate examination.

Respectfully submitted,



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Attachments: Cole, Backstrom, Later and Levin references

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